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| EXAMINER | |
|---|---|
| WEBB, WALTER E | |
| ART UNIT | PAPER NUMBER |
| 1612 | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/507,000 | REES ET AL. | |
| | Examiner | Art Unit | |
| | WALTER E. WEBB | 1612 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *20 April 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-8* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/3/2008, 7/27/2007, 1/3/2006, 9/23/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Election/Restrictions*

Applicant's election of sarsasapogenin as the active agent, ALS as the disease to be treated, neurotrophic factors as an additional active agent in the reply filed on 4/20/2009 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-8 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating non-cognitive neurodegeneration, does not reasonably provide enablement for **prevention** of non-cognitive neurodegeneration. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

To be enabling, the specification of the patent must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation. In re Wright, 999 F.2d 1557, 1561 (Fed. Cir. 1993). Explaining what is

meant by "undue experimentation," the Federal Circuit has stated:

> The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the claimed invention. PPG v. Guardian, 75 F.3d 1558, 1564 (Fed. Cir. 1996).[1]

The factors that may be considered in determining whether a disclosure would require undue experimentation are set forth by In re Wands, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing Ex parte Forman, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

1) the quantity of experimentation necessary,
2) the amount of direction or guidance provided,
3) the presence or absence of working examples,
4) the nature of the invention,
5) the state of the prior art,
6) the relative skill of those in the art,
7) the predictability of the art, and
8) the breadth of the claims.

These factors are always applied against the background understanding that scope of enablement varies inversely with the degree of unpredictability involved. In re Fisher, 57 CCPA 1099, 1108, 427 F.2d 833, 839, 166 USPQ 18, 24 (1970). Keeping that in mind, the Wands factors are relevant to the instant fact situation for the following reasons:

1. The nature of the invention, state and predictability of the art, and relative skill level

The invention relates to a method for the treatment or prevention of non-cognitive neurodegeneration. The relative skill of those in the art is high, that of an MD or PHD. That factor is outweighed, however, by the unpredictable nature of the art. As illustrative of the state of the art, the examiner cites Aminoff (The Western Journal of Medicine 1994). The prevention of Parkinson's disease is difficult since the cause is unknown (see pg. 307 at Preventive Treatment). The reference also teaches that despite relative success with pharmacotherapy such as levodopa, fluctuations in (or loss of) response may eventually occur (see abstract).

2. The breadth of the claims

Since the instant specification provides no limiting definition of the term "prevention", the term will be interpreted expansively. The term "prevention" may vary widely in meaning, from "preventing" a disease from occurring to "preventing" it from progressing. Nor is the term limited by any time frame.

The claims are thus very broad insofar as they suggest that one will not experience the disease when taking the claimed agent; that should one get the disease, it will not worsen; or that following its treatment, it will not recur. While such "prevention"

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[1] As pointed out by the court in In re Angstadt, 537 F.2d 498 at 504 (CCPA 1976), the key word is "undue", not "experimentation".

might theoretically be possible under strictly controlled laboratory conditions, as a practical matter it is nearly impossible to achieve in the "real world" in which patients live.

3. The amount of direction or guidance provided and the presence or absence of working examples

The specification provides no direction or guidance for practicing the claimed invention in its "full scope". No reasonably specific guidance is provided concerning useful therapeutic protocols for prevention of non-cognitive neurodegeneration, other than prevention of glutamate-induced neurodegeneration in rat model. The latter is corroborated by the working examples.

4. The quantity of experimentation necessary

Because of the known unpredictability of the art, and in the absence of experimental evidence, no one skilled in the art would accept the assertion that the instantly claimed agents could be predictably used to prevent non-cognitive neurodegeneration as inferred by the claim and contemplated by the specification. Accordingly, the instant claims do not comply with the enablement requirement of §112, since to practice the claimed invention in its "full scope" a person of ordinary skill in the art would have to engage in undue experimentation, with no reasonable expectation of

success.

**112, 2nd Paragraph**

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1) Claim 1 recites the phrase “A method for the treatment or prevention of, or in the preparation of compositions for the treatment of prevention of", which makes the claim ambiguous. The claim is so poorly constructed that it is impossible to determine exactly what is being recited. For the purpose of expediting prosecution, the claim will be interpreted as a method claim.

2) Claim 3 recites the limitation "formula Ia" in line 3. There is insufficient antecedent basis for this limitation in the claim.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-6 and 8 are rejected under 35 U.S.C. 102(b) as being anticipated by Xia et al. (GB 2 335 599, published 9/29/1999).

Xia et al. teaches a method of treating conditions that are characterized by a deficiency in the number and function of membrane bound receptors by administering saponins and sapogenins (see abstract). Disease conditions include include Alzheimer's disease, senile dementia, Parkinson's disease (**claim 8**), Lambert Eaton disease etc. (see id.). Saponins and sapogenins include sarsasapogenin (**claims 1-5**) (see id. and pg. 28, clm. 3 and 4). The composition is present with one or more additional active agents (**claim 6**) (see pg. 28, clm. 3).

### *Claim Rejections - 35 USC § 103*

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

1) Claim 7 is rejected under 35 U.S.C. 103(a) as being unpatentable over Xia et al. (*supra*) as applied to claims 1-6 and 8 above, and further in view of Aminoff (The Western Journal of Medicine 1994).

Xia et al. differs from the instant claims insofar as it does not teach adding a dopamine agonist for the treatment of Parkinson's disease.

Aminoff teaches treating Parkinson's disease with dopamine agonists (see Abstract). Aminoff does not teach the use of sarsasapogenin.

Generally, it is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose in order to form a third composition that is to be used for the very same purpose; the idea of combining them flows logically from their having been individually taught in prior art. See MPEP 2144.06. Thus, combining sarsasapogenin with a dopamine agonist as claimed in the instant invention would have been prima facie obvious since they are both taught to be useful for treating Parkinson's disease.

2) Claims 1-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Xia et al. (supra) in view of Louvel et al. (Trends in Pharmacological Sciences 1997).

Xia et al. teaches a method of treating conditions that are characterized by a deficiency in the number and function of membrane bound receptors by administering saponins and sapogenins (see abstract). The reference teaches that sarsasapogenin

(SaG), in particular, may be mediated through increases in the levels of one or more neurotrophic factors (see pg. 11, lines 30-31).

Xia et al. does not teach treatment of amyotrophic lateral sclerosis (ALS).

Louvel et al. teaches the use of neurotrophic factors in the treatment of ALS (see pg. 199, right col., last paragraph; see also pg. 202, left col. paragraphs 1-5). Louvel et al. does not teach the use of sarsasapogenin.

In KSR v. Telefex, 82 USPQ2d 1385, 1397 (U.S. 2007), the Supreme Court has held that when there is market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person has good reason to pursue known options within his or her technical grasp. Under these conditions, "obviousness to try" such options is permissible. In this instance, a market pressure exists in the medical/pharmaceutical industries to treat ALS using neurotrophic factors. Accordingly, it would have been obvious to have used sarsasapogenin in a method for treating ALS, since sarsasapogenin treats conditions that are characterized by a deficiency in the number and function of membrane bound receptors and mediates increases in the levels of one or more neurotrophic factors. It would have also been obvious to combine sarsasapogenin with neurtrophic factors since they would be used for the same purpose.

3) Claims 1-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Xia et al. (supra) in view of Roberts (US 4,831,033).

Xia et al., in addition to that taught above, also teaches that the sapogenin compounds treat Alzheimer's disease by selectively increasing muscarinic $M_1$ receptors (see pg. 23, lines 23-26), thereby increasing the activity of the neurotransmitter acetylcholine (see pg. 2, lines 5-21).

Xia et al. differs from the instant claims insofar as it does not teach treating ALS.

Roberts teaches that Alzheimer's disease is similar to ALS insofar as both are taught to be treated by increasing the activity of acetylcholine by administering a cholinesterase inhibitor that decreases its rate of breakdown (see Summary of the Invention at col. 3, lines 44-52; see also col. 3, lines 14-17).

Roberts does not teach the use of sarsasapogenin.

It would have been obvious to a person having ordinary skill in the art to use the sarsasapogenin of Xia et al. to treat ALS since ALS and Alzheimer's disease are known to be treated the same, as evidenced by Roberts. Since the sarsasapogenin of Xia et al. treats Alzheimer's disease by increasing the activity of acetylcholine through increased muscarinic receptors, it would have also been reasonably expected to treat ALS, which is also known to be treated via increased acetylcholine activity, also evidenced by Roberts.

It would have also been obvious to combine the sarsasapogenin of Xia et al. with the cholinesterase inhibitor of Roberts to treat ALS, since they would both serve to enhance of nerve function in the ALS patient.

## *Conclusion*

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Walter E. Webb whose telephone number is (571) 270-3287. The examiner can normally be reached on 8:00am-4:00pm Mon-Fri EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick F. Krass can be reached (571) 272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Walter E. Webb
/Walter E Webb/
Examiner, Art Unit 1612

/Frederick Krass/

Supervisory Patent Examiner, Art Unit 1612